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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,977	12/10/2003	Ann Wainright	127.00us	6435

33603 7590 08/06/2004

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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	

ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 08/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,977	WAINRIGHT ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 14-21 is/are allowed.

6)☒ Claim(s) 1-13 and 22-29 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 10 December 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 4, 5, and 8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Dadoo et al. (US 5,378,334), hereafter "Dadoo."

Addressing claim 1, Dadoo teaches a method for controlling an electric field in carrying out an electrophoretic process on a microfluidic device, the electric field capable of electrokinetically moving sample along the channel (abstract), the method comprising

applying an electric field to at least a first channel causing a sample to move towards a first location along the first channel (col. 7, ll. 45-50);

monitoring by optical detection the first location for at least a portion of the sample (col. 8, ll. 26-31); and

automatically modifying the electric field upon detecting the portion of the sample at the first location (col. 8, ln. 46 – col. 9, ln. 3, especially col. 8, ln. 57 – col. 9, ln. 3).

Addressing claims 2 and 28, Dadoo discloses at least absorbance and fluorescence monitoring (col. 8, ll.36-39).

Addressing claim 4, Dadoo discloses using an absorbance detector (col. 7, ll. 13-15).

Addressing claims 5 and 8, Dadoo discloses monitoring a plurality of locations with a different optical detector at each location (note detectors **22**, **228**, **228'**, and **222** in Figure 6).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-13 and 22-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramsey (EP 1162455 A1), hereafter "Ramsey."

Addressing claim 1, Ramsey teaches a method for controlling an electric field in carrying out an electrophoretic process on a microfluidic device, the electric field capable of electrokinetically moving sample along the channel (abstract), the method comprising

applying an electric field to at least a first channel causing a sample to move towards a first location along the first channel (paragraphs [0045] and [0046])

monitoring by optical detection the first location for at least a portion of the sample (paragraphs [0049], [0050]-[0053], and [0058]); and

modifying the electric field upon detecting the portion of the sample at the first location (paragraph [0047]).

Ramsey does not mention *automatically* modifying the electric field upon detecting the portion of the sample at the first location. In one embodiment the electric field is manually modified (paragraph [0068]).

First, 'It is well settled that it is not "invention" to broadly provide a mechanical or automatic means to replace manual activity which has accomplished the same result.' In re Venner et al., 120 USPQ 192, 194 quoting In re Rundell, 18 CCPA 1290, 48 F.2d 958, 9 USPQ 220.

Second, although Ramsey has one embodiment in which the electric field is manually modified, in at least one other embodiment the electric field is likely automatically modified because injection times ranged from 0.1 to 1.0 seconds (paragraph [0068]) and "an analysis could be performed every 4 s" (paragraph [0124]). Very few people have such quick reaction times, especially over a long duration.

Last, it would have been obvious to one with ordinary skill in the art at the time the invention was made to automatically modify the electric field upon detecting the portion of the sample at the first location because Ramsey teaches, "A smaller plug length leads to a higher separation efficiency and, consequently, to a greater component capacity for a given instrument and to higher speed separations" (paragraph [0055]) and that "floating" mode injection results in a temporal unstable injection plug (paragraph [0056] and Figure 9). Thus, one with ordinary skill in the art would recognize that it is desirable to be in run mode as soon as possible after injection mode. Even if "pinched" mode injection is used it would be desirable, in which the injected sample plug has temporal stability for at least one and one-half minutes (Figure 9), it would be desirable to automatically modify the electric field (to run mode) because after some time the

sample plug will start to diffuse, which will affect later separation, and because samples can be analyzed more quickly and accurately if the switching of the electric fields is performed automatically.

Addressing claim 2, Ramsey discloses at least fluorescence monitoring (paragraph [0056]).

Addressing claim 3, Ramsey discloses using a laser to illuminate the sample (paragraph [0040]).

Addressing claims 4 and 29, Ramsey discloses using a CCD camera (paragraph [0040]).

Addressing claim 5, although Ramsey does not mention monitoring a plurality of locations, this is implied because Ramsey states, "A charge coupled (CCD) camera was used to monitor designated **areas** of the chip and a photomultiplier tube (PMT) tracked single point events [emphasis added]"(paragraph [0040]). In any event, it would have been obvious to one with ordinary skill in the art at the time the invention was made to monitor a plurality of locations if there are a plurality of channel intersections in the microfluidic device because then the injections at each of the intersections could be automatically performed.

Addressing claim 6, Ramsey uses a single CCD camera to monitor several areas of the microfluidic device (paragraph [0040]. Also see paragraph [0086], which discloses single point detection at several locations).

Addressing claim 7, in Ramsey the detector comprises a CCD camera mounted on a stereo microscope (paragraph [0040]), which is usually movable so that it may be focused.

Addressing claim 8, although Ramsey only mentions one optical detector it would have been obvious to one with ordinary skill in the art at the time the invention was made to provide more than one detector if necessary to simultaneously monitor and automatically perform a plurality of injections.

Addressing claim 9, Ramsey discusses in detail an isotachophoresis (analyte stacking) embodiment (this begins on page 13).

Addressing claim 10, the isotachophoresis (analyte stacking) embodiment involves switching the voltage potential at various reservoirs (paragraph [0081], for example).

Addressing claim 11, Ramsey performs separation after stacking (paragraphs [0084] and [0086]).

Addressing claim 12, the electric field is modified after injection into the second (separation) channel so that separation of the injection sample plug may be performed (paragraph [0051]).

Addressing claims 13 and 27, a single point detection deice is disclosed (paragraph [0040]).

Addressing claim 22, Ramsey teaches a method for separating a plurality of components of a sample in a microfluidic device having a stacking channel and a separation channel downstream of the stacking channel, the method comprising

applying a first electric field to concentrate the components between a trailing electrolyte and a leading electrolyte along the stacking channel (paragraphs [0079] to [0083] and [0085]); and

applying a second electric field when at least a portion of the sample enters the separation channel whereby the components are separated by electrophoretic motilities along the channel (paragraphs [0084-[0086]).

Ramsey does not mention *automatically applying* the second electric field when the sample enters the separation channel. In one non-stacking embodiment the electric field is manually modified (paragraph [0068]).

First, 'It is well settled that it is not "invention" to broadly provide a mechanical or automatic means to replace manual activity which has accomplished the same result.' In re

Venner et al., 120 USPQ 192, 194 quoting In re Rundell, 18 CCPA 1290, 48 F.2d 958, 9 USPQ 220.

Second, although Ramsey has one non-stacking embodiment in which the electric field is manually modified, in at least one other embodiment the electric field is likely automatically applied because injection times ranged from 0.1 to 1.0 seconds (paragraph [0068]) and "an analysis could be performed every 4 s" (paragraph [0124]). Very few people have such quick reaction times, especially over a long duration.

Last, it would have been obvious to one with ordinary skill in the art at the time the invention was made to automatically apply the second electric field when the sample enters the separation channel because Ramsey teaches, "A smaller plug length leads to a higher separation efficiency and, consequently, to a greater component capacity for a given instrument and to higher speed separations" (paragraph [0055]). Thus, one with ordinary skill in the art would recognize that it is desirable to be in run (separation) mode as soon as possible after injection mode because after some time the sample plug will start to diffuse, which will affect later separation, and because samples can be analyzed more quickly and accurately if the switching of the electric fields is performed automatically.

Addressing claim 23, the stacking channel and separation channel are portions of the main channel (paragraphs [0080] and [0083]).

Addressing claim 24, electrodes in various reservoirs are activated (paragraph [0081] to [0083]).

Addressing claim 25, the electrodes appear to be removable as they are just wires placed in the reservoirs (paragraph [0030]).

Addressing claim 26, Ramsey does not mention whether the first electric field is modified when the detector senses the sample; however, as discussed in the rejection of claim 22 it would have been obvious to one with ordinary skill in the art at the time the invention was made to automatically apply the second electric field when the sample enters the separation channel.

7. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dadoo et al. (US 5,378,334), hereafter "Dadoo," in view of Hernandez (WO 92/13229 A2), hereafter "Hernandez."

Dadoo teaches a method for controlling an electric field in carrying out an electrophoretic process on a microfluidic device, the electric field capable of electrokinetically moving sample along the channel (abstract), the method comprising

applying an electric field to at least a first channel causing a sample to move towards a first location along the first channel (col. 7, ll. 45-50);

monitoring by optical detection the first location for at least a portion of the sample (col. 8, ll. 26-31); and

automatically modifying the electric field upon detecting the portion of the sample at the first location (col. 8, ln. 46 – col. 9, ln. 3, especially col. 8, ln. 57 – col. 9, ln. 3).

Dadoo also teaches at least absorbance and fluorescence monitoring (col. 8, ll.36-39).

Dadoo does not mention using inducing fluorescence with a laser; however, lasers were commonly used to induce fluorescence in capillary (microfluidic) electrophoresis systems at the time of the invention. Hernandez is one example (abstract). It would have been obvious to one with ordinary skill in the art at the time the invention was made to induce fluorescence with a laser as taught by Hernandez, for example, in the invention of Dadoo because a laser can be fine tuned to the particular wavelength for inducing fluorescence and it forms a narrow beam that can be precisely directed to region of the microfluidic device to be monitored.

Allowable Subject Matter

8. Claims 14-21 are allowed.

9. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 14: the nonobvious limitation in the combination of limitations is the requirement of "automatically applying a fourth voltage difference between the fourth reservoir and the fifth reservoir when the last component of the stacked sample reaches the fourth-channel intersection such that the components of the sample spatially separate while migrating along the first channel towards the fifth reservoir."

Ramsey does not disclose applying such a fourth voltage. In particular, the analyte stacking embodiment cannot apply the claimed fourth voltage because this embodiment uses a microfluidic device only having four reservoirs and three channels. The second and third channels intersect the first channel at the same intersection, so there is only one

one channel intersection. Thus, a fourth voltage cannot be automatically applied as claimed. See paragraph [0080] and Figure 12.

Williams et al. (US 2002/0079223 A1) discloses a stacking embodiment using a microfluidic device having five reservoirs (Figure 1B) and five channels, but there are only three spaced intersections. Thus, a fourth voltage cannot be automatically applied when the stacked sample reaches the fourth-channel intersection as claimed.

Similarly, Williams et al. (US 2002/0189946) discloses a stacking embodiment using a microfluidic device having five reservoirs (Figure 1B) and five channels, but with only three spaced intersections; and

b) Claims 15-21 depend directly or indirectly from allowable claim 14.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753
August 4, 2004